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Notebook #: 39040
CAI

EXHIBIT A

Measurement of SCH 58235 effects on Cholesterol absorption in ApoE KO and Normal Mice

Male ApoE knockout mice, age 6wks, were received from Jackson Laboratory along with age-matched C57BL/6 on 2-18-98. The mice were housed 5/cage, normal light cycle, normal diet.

On 3-6-98, 26 mice of each variety were weighed and housed 1/cage in suspended wire cages in rm GB-78 with normal light cycle, normal diet.

On 3-9-98 the mice were reweighed. Based on BW, the mice were divided into 5 groups for each type: Vehicle, SCH 58235 at 0.3, 1, 3, and 10 mg/kg per day.

Preparation of SCH 58235 soln based on 22g avg BW:

10mg/kg/day in 0.1ml corn oil: $2.2\text{mg/ml} \times 10\text{ml} = 22\text{mg}$ in 10ml corn oil

3mg/kg: 3 ml of 10mg/kg soln + 7 ml corn oil

1mg/kg: 3 ml of 3mg/kg soln + 6 ml corn oil

0.3mg/kg: 2 ml of 1mg/kg soln + 4.67 ml corn oil

The mice were gavaged using a 24ga feeding needle 30 min before receiving ^{14}C -cholesterol (NEN, NEC 018) and ^3H -sitosterol (NEN, CUS 030T). The radioactive soln was prepared:

114 μL ^3H -sitosterol stock (1 $\mu\text{Ci}/\mu\text{L}$ in EtOH)

1.425ml ^{14}C -cholesterol stock (40 $\mu\text{Ci}/\text{mL}$ in EtOH)

5.7 mg cholesterol, Sigma C 8667

5.7 mg β -sitosterol, Sigma S 1270

The soln was blown dry under N_2

5.7ml of corn oil was added, warmed to 60°C ; shaken for 1hr

Each 0.1ml dose contained: 1 μCi ^3H -sitosterol, 0.1mg cold sitosterol; 1 μCi ^{14}C -cholesterol, and 0.1mg cold cholesterol. Radioactive content was verified: 5 X 10 μL counted in Beckman LSC.

On 3-10, 3-11, and 3-12 feces were collected and stored at -20° in LSC vials just before dosing with vehicle or SCH 58235 late in the day.

Termination of the experiment on 3-13 involved BW detn, fecal collection followed by CO_2 inactivation, cardiac puncture blood sample, sacrifice by exsanguination, removal and weight of the liver. 3 X ~250mg pieces of liver were put in LSC vials. The liver samples were digested with 1ml of 1N NaOH at 60° overnight, neutralized with 0.1ml 12N HCl and counted. The blood samples were allowed to clot at room temp for 1hr, then centrifuged at 1000G for 15 min. The serum was analyzed for total cholesterol (Wako CII) and radioactivity (2 X 50 μL). Fecal samples were analyzed for radioactivity by combustion in a Packard Oxidizer.

PERFORMED BY *C. T. G. J. G.*

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READ AND UNDERSTOOD BY *Arthur B. B.*

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Sheet1

Mice transferred to wire cages & individually housed for acclimation: 3/6/98							
Body weights taken again on 3/9/98, mice grouped according to these BW							
SORT By Body Wt.							
C57/BLJ	BW(3-9)	Rank	Grp Mean	ApoE-KO	BW(3-9)	Rank	Grp Mean
10 8	24	5		4	23	5	
2	23.4	5		7 DEAD 3/10	22.7	5	
11	21.2	5		12	21.4	5	
17	20.3	5		(16)	17.2	5	
(18)	16.1	5	21.0	3	22.4	5	21.3
3 15	24.4	4		9	24.6	4	
5	23.4	4		8	22.7	4	
22	21.6	4		15	22	4	
20	20.7	4		13	21.5	4	
(12)	17.1	4	21.4	21	19.1	4	22.0
1 19	24.5	3		1	24.9	3	
3	23.2	3		19	22.5	3	
23	22	3		(26)	22.2	3	lost dead 3-11
(7)	20.8	3		10	21.7	3	
(6)	17.6	3	21.6	17	20.7	3	22.4
4	24.9	2		11	21.8	2	
16	23.1	2		5	25.3	2	
0.3 21	20.9	2		22	21.8	2	
(14)	18.8	2		24	21.2	2	
10	20.1	2	21.6	14	21.8	2	22.4
24	21.2	1		20	22.2	1	
1	25.8	1		6	25.4	1	
0 13	23	1		20	22.4	1	
9	22.9	1		18	22.3	1	
25	22.5	1		25	21.3	1	
(26)	14.4	1	21.7	(2)	16.8	1	21.8

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C57/BLJ & ApoE-KO Mouse									
Dual label CAL (3H-cholesterol, 14C-cholesterol)									
C57/BLJ					ApoE-KO				
#	BW3-6	BW3-9	BW3-13	A	#	BW3-6	BW3-9	BW3-13	A
8	25	24	25	1.0	4	23.5	23	23.5	0.5
3	21.2	23.4	22.9	-0.6	7	22.7	22.7		
11	22.8	21.2	22.3	1.1	3	22.1	22.4	22.3	-0.1
17	20.4	20.3	20.8	0.3	13	21.6	21.4	22.3	0.9
18	19.2	16.1	20	3.9	16	22	17.2	22.4	5.2
SCH 58235, 10mg/kg/day									
	21.7	21.0	22.1	1.1		22.4	21.3	22.6	1.6
	±1.0	±1.4	±0.9	±0.8		±0.3	±1.1	±0.3	±1.2
15	22.8	24.4	24	-0.4	9	25	24.6	25	0.4
5	22.2	23.4	23.8	0.5	8	23.2	22.7	23.5	0.8
22	22.2	21.6	17	-4.6	15	22.3	22	22.2	0.2
20	21.3	20.7	20	-0.7	12	21.7	21.5	21.6	0.1
12	21.7	17.1	23	5.9	21	18.6	19.1	18.6	0.4
SCH 58235, 3mg/kg/day									
	22.0	21.4	21.8	0.1		22.4	22.0	22.4	0.4
	±0.3	±1.3	±1.4	±1.7		±0.8	±0.9	±0.3	±0.1
19	24.8	24.5	25	0.5	1	24.6	24.9	23.8	-1.1
3	24.2	23.2	17.3	-9.9	18	21.5	22.5	21.8	-0.7
23	22.6	22	22.2	0.2	26	22.7	22.2		
7	23	20.8	19.6	-1.9	10	22.4	21.7	22.3	0.8
6	22.1	17.8	22.3	4.7	17	22	20.7	20.9	0.2
SCH 58235, 1mg/kg/day									
	22.8	21.8	21.3	-0.3		22.8	22.4	22.2	-0.2
	±0.6	±1.2	±1.3	±1.7		±0.6	±0.7	±0.6	±0.4
4	26.3	24.0	24.6	-0.3	5	26.2	25.3	24.8	-0.6
16	21.6	20.1	22.7	-0.4	11	21.5	21.8	19.4	-2.4
21	21.1	20.8	21.3	0.4	14	22	21.8	21.7	-0.1
18	21.1	20.1	20.6	0.5	22	22.3	21.8	22	0.2
14	24.8	18.8	23.6	4.8	24	21.4	21.2	20.3	-0.9
SCH 58235, 0.3mg/kg/day									
	22.0	21.6	22.8	1.0		22.7	22.4	21.6	-0.7
	±1.1	±1.1	±0.7	±1.0		±0.9	±0.7	±0.8	±0.5
1	24.5	25.8	19.3	-5.6	5	24.9	25.4	25.1	-0.3
18	18.7	28	23.3	0.3	20	22	22.4	21.6	-0.8
8	24.2	22.9	23.4	0.5	18	22.5	22.3	22.6	0.2
25	18.8	22.5	23.1	0.6	23	22.5	22.2	22.2	0.8
26	21.5	21.3	21.7	0.5	25	21.8	21.8	22	0.7
28	17.5	14.4	19.7	5.3	8	22.1	16.8	22.3	5.5
Vehicle, 0.1ml corn oil/day									
MEAN	20.9	21.8	21.8	0.1		22.5	21.7	22.5	0.9
	±1.2	±1.6	±0.8	±1.5		±0.6	±1.1	±0.8	±0.9

PERFORMED BY *C. Tetzlaff*

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CAI 3-9-98		MOUSE STUDY		TROL/CHOLESTEROL CHRONIC DOSING		
C57BL/6J		Serum		Total DPM	Liver	
#	treatment	³ H-DPM	¹⁴ C-DPM	³ H-DPM	¹⁴ C-DPM	Serum Cholesterol mg/dl
8	SCH 58235-10mg/kg			3589	3670	
2	SCH 58235-10mg/kg	192	30	1774	3079	85
11	SCH 58235-10mg/kg	25	62	2703	3551	87
17	SCH 58235-10mg/kg	201	148	6626	5992	85
18	SCH 58235-10mg/kg	90	72	1770	7013	79
15	SCH 58235-3mg/kg	92	149	1770	11456	83
5	SCH 58235-3mg/kg	52	193	3629	11359	73
22	SCH 58235-3mg/kg	128	67	30944	17258	76
20	SCH 58235-3mg/kg	8	138	3068	10111	76
12	SCH 58235-3mg/kg	499	114	3203	11335	97
19	SCH 58235-1mg/kg	87	212	3844	13972	92
3	SCH 58235-1mg/kg	79	253	2246	16032	82
23	SCH 58235-1mg/kg	153	165	1787	13805	70
7	SCH 58235-1mg/kg	143	162	5620	12779	83
6	SCH 58235-1mg/kg	211	279	4037	21194	94
4	SCH 58235-0.3mg/kg	102	1142	7280	45822	85
16	SCH 58235-0.3mg/kg	48	632	8437	32834	94
21	SCH 58235-0.3mg/kg	10	838	7550	53592	92
14	SCH 58235-0.3mg/kg	11	772	3582	46037	105
10	SCH 58235-0.3mg/kg	68	435	5794	22108	94
24	Vehicle, 0.1ml corn oil	43	1329	6202	81714	92
1	Vehicle, 0.1ml corn oil	627	832	11267	34738	128
13	Vehicle, 0.1ml corn oil	127	1249	5330	88089	96
9	Vehicle, 0.1ml corn oil	143	1423	2226	103754	86
25	Vehicle, 0.1ml corn oil	63	1518	14109	59724	100
26	Vehicle, 0.1ml corn oil	110	1842	13756	53361	122
ApoEKO						
4	SCH 58235-10mg/kg	803	713	7681	7491	546
12	SCH 58235-10mg/kg	127	298	2905	4377	829
16	SCH 58235-10mg/kg	65	367	3485	5483	579
3	SCH 58235-10mg/kg	89	1268	4530	14566	402
9	SCH 58235-3mg/kg	236	1235	5481	8088	587
8	SCH 58235-3mg/kg	268	631	4856	7796	409
15	SCH 58235-3mg/kg	146	986	4790	9613	481
13	SCH 58235-3mg/kg	301	961	4072	9943	443
21	SCH 58235-3mg/kg	335	1022	3794	7481	710
1	SCH 58235-1mg/kg	0	2368	9852	23280	405
18	SCH 58235-1mg/kg	0	2189	6309	31695	386
10	SCH 58235-1mg/kg	137	2710	4986	15097	847
17	SCH 58235-1mg/kg	57	1632	3341	21018	492
11	SCH 58235-0.3mg/kg	12	3621	11193	51090	416
5	SCH 58235-0.3mg/kg	446	7598	16426	52660	871
22	SCH 58235-0.3mg/kg	182	6840	10725	86583	718
24	SCH 58235-0.3mg/kg	269	5458	8579	40888	669
14	SCH 58235-0.3mg/kg	65	7868	7619	64917	705
8	Vehicle, 0.1ml corn oil	361	10133	15085	92537	663
20	Vehicle, 0.1ml corn oil	580	13554	35081	82942	753
23	Vehicle, 0.1ml corn oil	151	7552	28479	82301	523
18	Vehicle, 0.1ml corn oil	234	12690	19231	121537	616
25	Vehicle, 0.1ml corn oil	358	11760	17097	97945	772
2	Vehicle, 0.1ml corn oil	343	7741	19678	89954	739

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CAI 3-9-98		MOUSE STEROL/CHOLESTEROL CHRONIC DOSING			
C57/BLJ		Total DPM		Serum	
# treatment	³ H-DPM	¹⁴ C-DPM	³ H-DPM	¹⁴ C-DPM	Cholesterol mg/dL
Vehicle, 0.1ml corn oil					
mean	186	1332	8815	70230	104
sem	±90	±115	±2007	±10375	±7
SCH 58235-0.3mg/kg					
mean	48	764	6513	40079	94
sem	±17	±117	±853	±5597	±3
SCH 58235-1mg/kg					
mean	134	214	3507	15556	84
sem	±24	±23	±686	±1505	±4
SCH 58235-3mg/kg					
mean	156	132	2918	11065	81
sem	±88	±21	±401	±319	±4
without liver values from mouse #22					
SCH 58235-10mg/kg					
mean	127	78	3292	4661	84
sem	±42	±25	±699	±775	±2
ApoE KO					
Vehicle, 0.1ml corn oil					
mean	338	10572	22492	94536	677
sem	±59	±1035	±3129	±5915	±39
SCH 58235-0.3mg/kg					
mean	195	6237	11106	53230	676
sem	±77	±778	±1485	±3906	±74
SCH 58235-1mg/kg					
mean	49	2225	6072	22779	533
sem	±32	±225	±1339	±3438	±107
SCH 58235-3mg/kg					
mean	261	967	4610	8584	528
sem	±33	±97	±301	±499	±54
SCH 58235-10mg/kg					
mean	271	662	4650	7979	464
sem	±178	±222	±1065	±2288	±59

PERFORMED BY: *C. T. Telford*

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CAI 3-9-98		MOUSE SITOSTEROL/CHOLESTEROL CHRONIC DOSING			
CS7BL/J		% of Administered Dose			
		Serum		Liver	
#	Treatment	³ H-DPM	¹⁴ C-DPM	³ H-DPM	¹⁴ C-DPM
8	SCH 58235 10mg/kg			0.080	0.136
2	SCH 58235 10mg/kg	0.003	0.001	0.030	0.114
11	SCH 58235 10mg/kg	0.000	0.002	0.045	0.132
17	SCH 58235 10mg/kg	0.003	0.005	0.111	0.222
18	SCH 58235 10mg/kg	0.002	0.003	0.030	0.260
15	SCH 58235 1mg/kg	0.002	0.006	0.030	0.425
5	SCH 58235 1mg/kg	0.001	0.007	0.081	0.421
22	SCH 58235 1mg/kg	0.002	0.002	0.519	0.640
20	SCH 58235 1mg/kg	0.000	0.005	0.051	0.375
12	SCH 58235 1mg/kg	0.008	0.004	0.054	0.420
19	SCH 58235 1mg/kg	0.001	0.008	0.054	0.518
3	SCH 58235 1mg/kg	0.001	0.009	0.038	0.594
23	SCH 58235 1mg/kg	0.003	0.006	0.030	0.512
7	SCH 58235 1mg/kg	0.002	0.008	0.094	0.474
6	SCH 58235 1mg/kg	0.004	0.010	0.058	0.788
4	SCH 58235 1.3mg/kg	0.002	0.042	0.122	1.699
16	SCH 58235 1.3mg/kg	0.001	0.023	0.142	1.217
21	SCH 58235 1.3mg/kg	0.000	0.031	0.127	1.987
14	SCH 58235 1.3mg/kg	0.000	0.029	0.030	1.707
10	SCH 58235 1.3mg/kg	0.001	0.016	0.098	0.820
24	Vehicle, 0.1ml corn oil	0.001	0.049	0.104	3.030
1	Vehicle, 0.1ml corn oil	0.011	0.031	0.189	1.288
13	Vehicle, 0.1ml corn oil	0.002	0.046	0.089	3.266
9	Vehicle, 0.1ml corn oil	0.002	0.053	0.097	3.847
25	Vehicle, 0.1ml corn oil	0.001	0.055	0.237	2.214
26	Vehicle, 0.1ml corn oil	0.002	0.061	0.231	1.978
ApoE KO					
4	SCH 58235 0mg/kg	0.013	0.026	0.129	0.278
12	SCH 58235 0mg/kg	0.002	0.011	0.049	0.162
16	SCH 58235 0mg/kg	0.001	0.014	0.058	0.203
3	SCH 58235 0mg/kg	0.001	0.047	0.076	0.540
8	SCH 58235 1mg/kg	0.004	0.048	0.092	0.300
8	SCH 58235 1mg/kg	0.005	0.023	0.082	0.288
15	SCH 58235 1mg/kg	0.002	0.037	0.060	0.356
13	SCH 58235 1mg/kg	0.005	0.036	0.068	0.368
21	SCH 58235 1mg/kg	0.006	0.038	0.064	0.277
1	SCH 58235 1mg/kg	0.000	0.088	0.152	0.883
19	SCH 58235 1mg/kg	0.000	0.081	0.106	1.176
10	SCH 58235 1mg/kg	0.002	0.100	0.084	0.560
17	SCH 58235 1mg/kg	0.001	0.061	0.056	0.779
11	SCH 58235 1.3mg/kg	0.000	0.134	0.168	1.894
5	SCH 58235 1.3mg/kg	0.007	0.282	0.276	1.952
22	SCH 58235 1.3mg/kg	0.003	0.246	0.180	2.088
24	SCH 58235 1.3mg/kg	0.005	0.202	0.161	1.516
14	SCH 58235 1.3mg/kg	0.001	0.292	0.128	2.407
6	Vehicle, 0.1ml corn oil	0.006	0.378	0.253	3.431
20	Vehicle, 0.1ml corn oil	0.010	0.503	0.588	3.075
23	Vehicle, 0.1ml corn oil	0.003	0.280	0.478	3.051
18	Vehicle, 0.1ml corn oil	0.004	0.470	0.323	4.506
25	Vehicle, 0.1ml corn oil	0.006	0.436	0.292	3.631
2	Vehicle, 0.1ml corn oil	0.008	0.287	0.330	3.395

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CAI 3-9-98		MOUSE SI OSTEROL/CHOLESTEROL CHRONIC DOSING			
C57BL/6J		% of Radioactivity administered			
		erum		Liver	
treatment		³ H	¹⁴ C	³ H	¹⁴ C
Vehicle, 0.1ml corn oil					
mean		0.003	0.05	0.15	2.60
sem		±0.002	±0.00	±0.03	±0.38
SCH 58235-0.3mg/kg					
mean		0.001	0.03	0.11	1.49
sem		±0.000	±0.00	±0.01	±0.21
SCH 58235-1mg/kg					
mean		0.002	0.01	0.05	0.58
sem		±0.000	±0.00	±0.01	±0.06
SCH 58235-3mg/kg					
mean		0.003	0.005	0.14	0.46
sem		±0.001	±0.001	±0.03	±0.05
SCH 58235-10mg/kg					
mean		0.002	0.003	0.08	0.17
sem		±0.001	±0.001	±0.02	±0.03
ApoE KO					
Vehicle, 0.1ml corn oil					
mean		0.006	0.395	0.40	3.52
sem		±0.001	±0.047	±0.06	±0.27
SCH 58235-0.3mg/kg					
mean		0.003	0.231	0.13	1.97
sem		±0.001	±0.023	±0.02	±0.14
SCH 58235-1mg/kg					
mean		0.001	0.082	0.10	0.84
sem		±0.001	±0.008	±0.02	±0.13
SCH 58235-3mg/kg					
mean		0.004	0.036	0.08	0.32
sem		±0.001	±0.004	±0.01	±0.02
SCH 58235-10mg/kg					
mean		0.005	0.025	0.08	0.30
sem		±0.003	±0.008	±0.02	±0.08

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CAI 3-9-98		MOUSE		STOSTEROL/CHOLESTEROL CHRONIC DOSING				FECES	
				% Radioactivity administered					
DAY 1				DAY 1					
C57BL/J				¹⁴ C-dpm		¹⁴ C		³ H-dpm	
#	a	b		dpm	%	a	b	dpm	%
8	987125			887033	32.8	2025421		2025331	34.0
2	975421	88:719		1861047	69.0	2258000	1886947	4244857	71.2
11	783937	102:322		1810768	67.1	1854147	2928770	4182827	70.2
17	358181			358068	13.3	889851		889861	14.9
18	992898			992803	38.8	2313066		2312976	38.8
19	2128251			2128164	78.9	5370708		5370618	80.1
5	1641868			1641775	60.9	4087620		4087530	68.6
23	23053			22660	0.9	23663		23573	0.4
28	1082450	98:328		2048386	76.0	2598855	2249145	4845910	81.3
12	1718945			1718852	63.7	4545208		4545118	76.2
13	1786223			1786180	65.5	4782818		4782728	80.2
3	1854941			1854848	68.6	4755250		4755160	79.8
23	1419594			1419501	62.6	3891158		3891078	61.9
7	92109			92016	3.4	266301		266211	4.5
6	1893467			1893364	70.2	4410592		4410502	74.0
4	1357988			1357876	50.3	4859352		4859262	81.6
16	1285373			1285280	47.8	4300444		4300354	72.3
21	1501587			1501464	65.7	5427541		5427451	91.0
14	1122234			1122141	41.8	4158850		4158760	68.8
10	1367878			1367788	50.7	4385834		4385744	73.7
24	829534			829441	20.8	4265085		4264995	71.5
1	74080			73987	2.7	344074		343984	5.8
13	621682			621589	23.0	4441072		4440982	74.5
9	542967			542874	20.1	3878758		3878668	81.7
26	775384			775291	28.7	4732673		4732583	79.4
26	620288			620195	30.4	4838792		4838702	81.2
DAY 1				DAY 1					
ApoE KO				¹⁴ C-dpm		¹⁴ C		³ H-dpm	
#	a	b		dpm	%	a	b	dpm	%
4	68731			66636	2.5	156483		156373	2.6
7	434470			434377	18.1	1045418		1045328	17.5
12	1669636			1669542	81.9	4131861		4131871	69.3
16	1327886			1327802	49.9	2895223		2895133	50.2
3	1447442			1447348	53.7	3645363		3645273	61.2
8	1782195			1782102	63.4	4290282		4290192	72.0
8	2086858			2086766	77.8	4972338		4972248	83.4
15	1029296	742:30		1771333	65.7	2459934	1808870	4260714	71.8
13	1878821			1878728	69.7	4708750		4708660	79.0
21	1869088			1868995	79.0	4820198		4820108	77.5
1	933982	828:16		1583285	68.0	2881014	1740882	4421906	74.2
18	886519	616:16		1601782	59.4	3126043	1702709	4828661	81.0
26	834846			834753	23.6	1815768		1815678	30.6
10	885834	892:18		1847030	68.5	2457416	2115450	4572776	78.7
17	1893528			1893536	73.0	5462382		5462292	81.6
11	1895844			1895851	81.8	4748920		4748830	79.8
6	1432036			1431943	53.1	4766683		4766593	80.0
22	1157308			1157215	42.0	4198382		4198292	70.4
24	1142145			1142052	42.3	3812484		3812394	64.0
14	1354544			1354451	50.2	4909010		4908920	62.3
8	727382			727289	27.0	4246164		4246074	71.2
28	626006	333:10		850062	31.8	2809208	1717769	4520885	75.8
23	648912			648819	24.1	4584285		4584195	76.8
10	548786			548693	20.3	8588716		8588626	60.4
28	483518			483425	17.2	4380620		4380530	76.3
2	1042868	888:10		1108495	41.1	4491404	186339	4588644	75.8

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CAI 3-9-98				MOUSE SITOSTEROL				CHOLESTEROL CHRONIC DOSING					
% of Radioactivity administered													
DAY 2				DAY 2									
C57BL/J													
#	a	b	dpm	%	a	b	dpm	%	a	b	dpm	%	%
8	101453		1013	3.8	110529		110439	1.9					
2	99217		99	3.7	91423		91403	1.5					
11	129380		129	4.8	235560		235490	4.0					
17	108957	81813	100	7.1	189818	144990	334718	5.8					
18	1059949		1059	99.8	2293715		2293625	38.5					
15	62152	42984	105	3.9	27091	14193	41184	0.7					
5	116004		116	4.3	141156		141056	2.4					
22	12112		12	0.4	14228		14198	0.2					
20	56995		56	2.1	19256		18166	0.3					
12	183309	83024	266	9.9	270951	74712	344973	6.8					
19	126290	67248	192	7.2	193006	24155	157071	2.6					
3	120207		120	4.8	70983		70863	1.2					
23	174876		174	6.5	177141		177051	3.0					
7	284632		284	10.6	742171		742081	12.4					
6	169423		169	6.3	210650		210560	3.5					
4	140934		140	5.2	68028		67938	1.1					
16	113118	49310	182	6.0	32640	12986	45636	0.8					
21	130916		130	4.8	93968		93878	0.6					
14	195922		195	7.3	319088		318998	5.4					
10	127151		127	4.7	33821		33601	0.6					
24	138881		138	5.1	136068		135808	2.3					
1	37548		37	1.4	261843		261853	4.4					
13	110292	56870	167	6.2	37957	20188	58035	1.0					
9	180874		180	5.0	43698		43608	0.7					
25	202150		202	7.5	145620		145530	2.4					
26	568832		568	21.1	961737		961667	16.1					
DAY 2				DAY 2									
APOE KO													
#	a	b	dpm	%	a	b	dpm	%	a	b	dpm	%	%
4	35174		35	1.3	72811		72721	1.2					
7													
12	250770		250	9.3	358648		358558	6.0					
16	287924	170950	458	17.0	569916	328878	898754	15.1					
3	167828		167	6.2	348814		348784	5.8					
8	177982		177	6.6	318031		317931	5.3					
6	186630	33337	219	8.2	362130	8855	371864	6.2					
15	43101	36788	79	3.0	23830	22288	45129	0.8					
13	131778		131	4.9	234422		234402	3.9					
21	114420	39864	154	5.7	185078	29877	214895	3.6					
1	75668		75	2.9	41028		40919	0.7					
18	62881	44468	107	4.0	18714	12242	31824	0.5					
26					980635		980565	16.4					
10	71860		71	2.7	40603		40593	0.7					
17	107272		107	4.0	40202		40192	0.7					
11	100716		100	3.7	22419		22359	0.4					
5	119887		119	4.4	68762		68662	1.2					
22	123838	88236	209	7.8	165810	69585	174825	2.9					
24	148084		147	5.5	373012		372812	6.3					
14	60508	55028	115	4.3	34001	25778	59888	1.0					
6	111293	89292	209	7.4	128012	82883	210522	3.6					
20	108348	153808	2620	9.7	225517	20061	426518	7.1					
23	89433	63144	1524	5.7	108615	28752	139239	2.3					
18	126178		126	4.7	190215		190146	1.7					
25	154024		154	5.7	166605		166788	2.8					
2	73269	85189	188	5.9	98874	130322	230103	3.9					

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CAI 3-9-98			TOSTEROL/CHOLESTEROL CHRONIC DOSING							
% of Radioactivity			Uninjected		DAY 3		FECES			
DAY 3			C-14 dpm		H-3 dpm					
C57BL/J			a		b					
#	a	b	dpm	%	dpm	%	dpm	%	dpm	%
1	18011		17921	0.7	3405				3315	0.1
2	19336		18246	0.7	3315				3223	0.1
11	25846		26756	1.0	34519				34428	0.8
17	22585	12	34675	1.3	42413		24786		67108	1.1
18	86562		86472	3.2	98613				98523	1.7
19	27399		27309	1.0	4073				3983	0.1
20	10954		54156	2.0	64509				64419	1.1
22	28838		10884	0.4	15214				15124	0.9
20	30303	1524	22745	0.8	3497				3407	0.1
18	30644		182675	6.8	18859		822796		839565	14.1
9	39240		30554	1.1	3736				3646	0.1
23	124373		35160	1.3	7356				7266	0.1
7	23449		124283	4.8	243315				243225	4.1
6	28208	192	23358	0.9	21687				21497	0.4
4	38444	334	48108	1.8	5198		3563		3672	0.1
16	33938	549	71810	2.7	2848		6818		8377	0.1
21	45847	387	88831	3.9	11272		97786		108978	1.8
14	49427	403	84510	3.1	5060		4228		9199	0.2
19	33950	277	89671	3.8	18550		16498		34968	0.6
24	84132		81635	2.3	4910		2781		7811	0.1
1	16655		84042	3.1	49044				48954	0.8
13	74807	467	16585	0.6	31752				31682	0.5
9	90784		121478	4.5	14056		6190		20156	0.3
25	90878		90694	3.4	10922				10832	0.2
26	118387		90788	3.4	16533				16443	0.9
			116287	4.3	66018				65928	1.1
DAY 3			C-14 dpm		H-3 dpm					
ApoE KO			a		b					
#	a	b	dpm	%	dpm	%	dpm	%	dpm	%
4	5500	400	8507	0.2	15626		12355		27891	0.5
12	17773	1218	29885	0.5	12107		8453		20470	0.3
16	12884	1309	25864	0.4	11501		12833		24344	0.4
3	16465	1341	29782	0.5	18621		10884		28818	0.5
8	9812	1284	22468	0.4	4595		5404		10008	0.2
15	13843	841	22264	0.4	2204		1876		3689	0.1
13	14103	1003	24051	0.4	3258		8102		5270	0.1
21	14805	1121	26026	0.4	10420		6955		17285	0.3
1	13451	860	22056	0.4	11024		7384		18528	0.3
19	20808	1884	39566	0.7	8072		3147		11129	0.2
26	45008		44818	0.8	10606				10518	0.2
10	12101	683	20844	0.3	2062		1800		3872	0.1
17	33366		39278	0.6	4084				4894	0.1
11	32142	25554	57608	1.0	6922		4451		10193	0.2
6	27272	18301	45483	0.8	8116		8103		16219	0.3
22	26543	24012	80585	1.0	18810		7102		23822	0.4
24	48383		49283	0.8	90344				90254	1.5
14	31118	17403	48431	0.8	7258		3306		10554	0.2
8	34293	22732	66876	1.0	10386		8306		18673	0.3
20	98444		99354	1.7	256801				256711	4.3
23	43689	33381	77160	1.3	15480		8584		24884	0.4
18	37108	19801	56819	1.0	17120		8848		25878	0.4
25	36987	20288	58562	0.9	30621		17364		47836	0.8
2	22358	25388	57624	1.0	26272		10385		35877	0.6

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MOUSE CAI 3-98 FECAL RADIOACTIVITY									
C57BL/J									
Total % Administered									
#	¹⁴ C-dpm	³ H-dpm	mean(¹⁴ C)	³ H:sem	Absorbed	mean	sem	Rx	
8	37.3	35.9	58	±11.5	-3.97	-0.54	±1.02	SCH 58235	
2	73.4	72.8	56	±11.7	-0.81			10mg/kg/day	
11	72.9	74.7			2.38				
17	21.6	21.7			0.18				
18	79.3	78.0			-0.47				
15	83.8	80.9	62	±15.4	7.76	8.66	±2.78	SCH 58235	
5	67.2	72.0	59	±17.3	6.73			3mg/kg/day	
22	1.7	0.9							
20	78.9	81.7			3.33				
12	80.4	88.1			16.38				
19	73.8	82.9	61	±11.8	11.03	6.38	±2.51	SCH 58235	
3	74.8	81.1	65	±12.3	7.88			1mg/kg/day	
23	63.7	69.0			7.62				
7	14.8	17.3							
8	78.8	77.7			-0.76				
4	58.2	82.8	57	±1.8	20.67	27.53	±1.82	SCH 58235	
16	57.1	74.9	79	±3.3	23.78			0.3mg/kg/day	
21	83.6	91.8			30.67				
14	52.2	75.7			31.06				
19	57.7	74.4			22.47				
24	39.0	74.7	33	±8.8	47.74	51.15	±1.97	Vehicle	
1	4.7	10.7	87	±12.3	58.62			1ml corn oil/day	
13	33.7	75.8			55.49				
9	29.4	62.6			52.99				
25	38.6	82.1			51.77				
26	55.8	98.4			43.29				
ApoE KO									
Total % Administered									
#	¹⁴ C-dpm	³ H-dpm	mean(¹⁴ C)	³ H:sem	Absorbed	mean	sem	Rx	
4	9.9	4.3	59	±15.7		4.79	±3.45	SCH 58235	
7			53	±16.5				10mg/kg/day	
12	71.7	76.7			6.26				
16	66.7	65.7			-1.40				
3	60.4	67.5			10.51				
9	72.3	77.5	78	±3.0	6.82	5.58	±1.24	SCH 58235	
8	85.3	89.7	80	±2.9	3.76			3mg/kg/day	
16	89.0	72.5			4.79				
13	75.0	83.2			9.89				
21	79.1	81.4			2.85				
1	61.5	75.1	68	±3.8	18.01	15.58	±2.95	SCH 58235	
19	84.1	81.7	81	±3.8	21.55			1mg/kg/day	
26									
10	71.5	77.5			7.65				
17	78.4	82.4			15.10				
11	58.4	80.2	54	±1.7	28.60	30.77	±9.97	SCH 58235	
5	58.3	81.4	78	±2.3	28.38			0.3mg/kg/day	
22	51.7	73.8			29.91				
24	48.7	71.7			32.17				
14	65.3	83.5			33.78				
6	35.4	75.1	34	±3.9	52.81	55.52	±4.18	Vehicle	
20	43.2	87.3	77	±3.4	60.47			1ml corn oil/day	
23	31.0	79.2			60.80				
18	29.9	82.5			58.55				
25	23.8	78.9			70.18				
2	48.0	60.1			40.08				

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